

FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO. 0609.4280001	APPLICATION NO. 08/896,053
		APPLICANT JANSSENS et al.	
		FILING DATE July 17, 1997	GROUP 1808

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
ANP62	AA1 5,485,827	01/23/1996	Zapol et al.			02/10/1995
	AB1 5,498,539	03/12/1996	Harrison et al.			07/02/1992
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
AL						Yes No
AM						Yes No
AN						Yes No
AO						Yes No
AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	1	Adnot, S., et al., "Loss of Endothelium-dependent Relaxant Activity in the Pulmonary Circulation of Rats Exposed to Chronic Hypoxia," <i>J. Clin. Invest.</i> 87:155-162 (1991).
	AS	1	Assender, J.W., et al., "Does Nitric Oxide Inhibit Smooth Muscle Proliferation?," <i>J. Cardiovasc. Pharmacol.</i> 17(Suppl. 3):S104-S107 (1991).
	AT	1	Bernstein, A., et al., "Gene Transfer with Retrovirus Vectors," in: <i>Genetic Engineering: Principles and Methods</i> , Volume 7, Setlow, J.K., and Hollaender, A., eds., Plenum Press; New York, pp. 235-261 (1985).

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	AO						Yes No
	AP						Yes No

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<i>PHB</i>	AR	2	Bredt, D.S., et al., "Localization of nitric oxide synthase indicating a neural role for nitric oxide," <i>Nature</i> 347:768-770 (1990).
<i>J</i>	AS	2	Cline, M.J., "Perspectives for Gene Therapy: Inserting New Genetic Information into Mammalian Cells by Physical Techniques and Viral Vectors," <i>Pharmac. Ther.</i> 29:69-92 (1985).
<i>V</i>	AT	2	Cohen, A.H., et al., "Inhibition of Cyclic 3'-5'-Guanosine Monophosphate-specific Phosphodiesterase Selectively Vasodilates the Pulmonary Circulation in Chronically Hypoxic Rats," <i>J. Clin. Invest.</i> 97(1):172-179 (January 1996).

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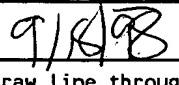
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	AR	3	de Graaf, J.C., <i>et al.</i> , "Nitric Oxide Functions as an Inhibitor of Platelet Adhesion Under Flow Conditions," <i>Circulation</i> 85:2284-2290 (1992).				
	AS	3	Dick, J.E., <i>et al.</i> , "Genetic manipulation of hematopoietic stem cells with retrovirus vectors," <i>Trends in Genetics</i> 2:165-170 (1986).				
	AT	3	Frostell, C.G., <i>et al.</i> , "Inhaled Nitric Oxide Selectively Reverses Human Hypoxic Pulmonary Vasoconstriction without Causing Systemic Vasodilation," <i>Anesthesiology</i> 78(3):427-435 (1993).				

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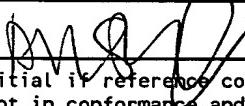
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	AR	4	Furchtgott, R.F., and Vanhoutte, P.M., "Endothelium-derived relaxing and contracting factors," FASEB J. 3:2007-2018 (1989).
	AS	4	Garg, U.C., and Hassid, A., "Nitric Oxide-generating Vasodilators and 8-Bromo-Cyclic Guanosine Monophosphate Inhibit Mitogenesis and Proliferation of Cultured Rat Vascular Smooth Muscle Cells," J. Clin. Invest. 83:1774-1777 (1989).
	AT	4	Giaid, A., and Saleh, D., "Reduced Expression of Endothelial Nitric Oxide Synthase in the Lungs of Patients with Pulmonary Hypertension," N. Engl. J. Med. 333(4):214-221 (July 1995).

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<i>PNB</i>	AR	5	Girard, C., et al., "Inhaled Nitric Oxide after Mitral Valve Replacement in Patients with Chronic Pulmonary Artery Hypertension," <i>Anesthesiology</i> 77:880-883 (1992).
<i>V</i>	AS	5	Gómez-Foix, A.M., et al., "Adenovirus-mediated Transfer of the Muscle Glycogen Phosphorylase Gene into Hepatocytes Confers Altered Regulation of Glycogen Metabolism," <i>J. Biol. Chem.</i> 267(35):25129-25134 (1992).
<i>V</i>	AT	5	Hazinski, T.A., et al., "Localization and Induced Expression of Fusion Genes in the Rat Lung," <i>Am. J. Respir. Cell Mol. Biol.</i> 4:206-209 (1991).

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<i>DHS</i>	AR	<u>6</u>	Heath, D., "The pathology of pulmonary hypertension," <i>Eur. Respir. Rev.</i> 3(16):555-558 (1993).
<i>V</i>	AS	<u>6</u>	Hibbs, J.B., Jr., et al., "Nitric Oxide: A Cytotoxic Activated Macrophage Effector Molecule," <i>Biochem. Biophys. Res. Comm.</i> 157(1):87-94 (1988).
<i>V</i>	AT	<u>6</u>	Ignarro, L.J., "Endothelium-derived nitric oxide: actions and properties," <i>FASEB J.</i> 3:31-36 (1989).

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<i>DMSB</i>	AR	7	Janssens, S.P., <i>et al.</i> , "Cloning and Expression of a cDNA Encoding Human Endothelium-derived Relaxing Factor/Nitric Oxide Synthase," <i>J. Biol. Chem.</i> 267(21):14519-14522 (1992).
<i>✓</i>	AS	7	Janssens, S.P., <i>et al.</i> , "Functional and structural changes with hypoxia in pulmonary circulation of spontaneously hypertensive rats," <i>J. Applied Physiol.</i> 77(3):1101-1107 (1994).
<i>✓</i>	AT	7	Janssens, S.P., <i>et al.</i> , "Adenoviral-mediated Transfer of the Human Endothelial Nitric Oxide Synthase Gene Reduces Acute Hypoxic Pulmonary Vasoconstriction in Rats," <i>J. Clin. Invest.</i> 98(2):317-324 (July 1996).

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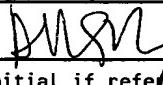
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	AR	8	Johns, R.A., et al., "Endothelium-Dependent Relaxation and Cyclic GMP Accumulation in Rabbit Pulmonary Artery Are Selectively Impaired by Moderate Hypoxia," Circ. Res. 65:1508-1515 (1989).
	AS	8	Kawai, N., et al., "Constitutive endothelial nitric oxide synthase gene expression is regulated during lung development," Am. J. Physiol. 268:L589-L595 (April 1995).
	AT	8	Kiem, H.-P., et al., "Gene therapy and bone marrow transplantation," Curr. Opin. Oncol. 7(2):107-114 (March 1995).

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<i>PN/SN</i>	AR	9	Lowenstein, C.J., et al., "Cloned and expressed macrophage nitric oxide synthase contrasts with the brain enzyme," Proc. Natl. Acad. Sci. USA 89:6711-6715 (1992).
<i>J</i>	AS	9	Marletta, M.A., "Nitric oxide: biosynthesis and biological significance," Trends Biochem. Sci. 14:488-492 (1989).
<i>J</i>	AT	9	McQuillan, L.P., et al., "Hypoxia inhibits expression of eNOS via transcriptional and posttranscriptional mechanisms," Am. J. Physiol. 267:H1921-H1927 (1994).

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<i>MBS</i>	AR	<u>10</u>	Miller, A.D., "Human gene therapy comes of age," <i>Nature</i> 357:455-460 (1992).
<i>J</i>	AS	<u>10</u>	Moncada, S., <i>et al.</i> , "Nitric Oxide: Physiology, Pathophysiology, and Pharmacology," <i>Pharmacol. Rev.</i> 43:109-142 (1991).
<i>J</i>	AT	<u>10</u>	Morrow, J.F., "The Prospects for Gene Therapy in Humans," <i>Ann. N.Y. Acad. Sci.</i> 265:13-21 (1976).

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>BSB</i>	AR	<u>11</u>	Nathan, C., "Nitric oxide as a secretory product of mammalian cells," FASEB J. 6:3051-3064 (1992).
<i>J</i>	AS	<u>11</u>	Pepke-Zaba, J., et al., "Inhaled nitric oxide as a cause of selective pulmonary vasodilatation in pulmonary hypertension," Lancet 338:1173-1174 (1991).
<i>J</i>	AT	<u>11</u>	Radomski, M.W., et al., "The Role of Nitric Oxide and cGMP in Platelet Adhesion to Vascular Endothelium," Biochem. Biophys. Res. Comm. 148(3):1482-1489 (1987).

EXAMINER *DMS/BSB* DATE CONSIDERED *9/16/98*

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<i>DNSB</i>	AR	<u>12</u>	Rimar, S., and Gillis, N.C., "Selective Pulmonary Vasodilation by Inhaled Nitric Oxide Is Due to Hemoglobin Inactivation," <i>Circulation</i> 88(6):2884-2887 (1993).
<i>V</i>	AS	<u>12</u>	Roberts, J.D., et al., "Inhaled nitric oxide in persistent pulmonary hypertension of the newborn," <i>Lancet</i> 340:818-819 (1992).
<i>V</i>	AT	<u>12</u>	Roberts, J.D., Jr., et al., "Continuous Nitric Oxide Inhalation Reduces Pulmonary Arterial Structural Changes, Right Ventricular Hypertrophy, and Growth Retardation in the Hypoxic Newborn Rat," <i>Circ. Res.</i> 76(2):215-222 (February 1995).

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<i>DRS</i>	AR	<u>13</u>	Rossaint, R., et al., "Inhaled Nitric Oxide for the Adult Respiratory Distress Syndrome," <i>N. Engl. J. Med.</i> 328(6):399-405 (1993).
<i>DRS</i>	AS	<u>13</u>	Salser, W., et al., "Gene Therapy Techniques: Use of Drug Resistance Selections in Intact Animals to Insert Human Globin Genes Into Bone-Marrow Cells of Living Mice," in: <i>Organization and Expression of Globin Genes</i> , Stamatoyannopoulos, G., and Nienhuis, A.W., eds., Alan R. Liss, Inc., pub., New York, N.Y., p. 313-334 (1981).
	AT	<u>13</u>	A copy of the original paper must be included Setoguchi, Y., et al., "Transfer of endothelial nitric oxide synthase gene in the purpose of gene therapy for pulmonary arterial hypertension," <i>Nippon Rinsho Jap. J. Clin. Med.</i> 54(2):369-76 (February 1996), English language abstract, Medline database accession no. 96435198.

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<i>DMS</i>	AR	<u>14</u>	Shaul, P.W., et al., "Acute and Prolonged Hypoxia Attenuate Endothelial Nitric Oxide Production in Rat Pulmonary Arteries by Different Mechanisms," <i>J. Cardiovasc. Pharmacol.</i> 22:819-827 (1993).
<i>✓</i>	AS	<u>14</u>	Stribling, R., et al., "Aerosol gene delivery <i>in vivo</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 89:11277-11281 (1992).
<i>✓</i>	AT	<u>14</u>	Stuehr, D.J., and Griffith, O.W., "Mammalian Nitric Oxide Synthases," <i>Adv. Enzymol. Relat. Areas Mol. Biol.</i> 65:287-346 (1992).

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	15	Must Submit an actual copy of the paper Tzeng, E., et al., "Vascular gene transfer of the human inducible nitric oxide synthase: characterization of activity and effects on myointimal hyperplasia," <i>Molec. Med.</i> 2(2):211-225 (March 1996), abstract, Medline database accession no. 96295016.
	AS	15	Vanhoutte, P.M., "The Endothelium - Modulator of Vascular Smooth-Muscle Tone," <i>N. Engl. J. Med.</i> 319:512-513 (1988).
	AT	15	von der Leyen, H.E., et al., "Gene therapy inhibiting neointimal vascular lesion: <i>In vivo</i> transfer of endothelial cell nitric oxide synthase gene," <i>Proc. Natl. Acad. Sci. USA</i> 92:1137-1141 (February 1995).

EXAMINER  DATE CONSIDERED 9/18/98

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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO. 0609.4280001	APPLICATION NO. 08/896,053
		APPLICANT JANSSENS et al.	
		FILING DATE July 17, 1997	GROUP 1808

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
AA							
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AO							Yes No
AP							Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>MSB</i>	AR	16	Xue, C., et al., "Distribution of NOS in normoxic vs. hypoxic rat lung: upregulation of NOS by chronic hypoxia," Amer. J. Physiol. 267:L667-L678 (1994).
	AS		
	AT		

EXAMINER *MSB* DATE CONSIDERED 9/18/98

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